

Simultaneous Venous-Arterial Doppler Ultrasound During Early Fluid Resuscitation to Characterize a Novel Doppler Starling Curve: A Prospective Observational Pilot Study

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Abstract

Background: The likelihood of a patient being preload responsive—a state where the cardiac output or stroke volume (SV) increases significantly in response to preload—depends on both cardiac filling and function. This relationship is described by the canonical Frank-Starling curve. **Research Question:** We hypothesize that a novel method for phenotyping hypoperfused patients (ie, the “Doppler Starling curve”) using synchronously measured jugular venous Doppler as a marker of central venous pressure (CVP) and corrected flow time of the carotid artery (ccFT) as a surrogate for SV will refine the pretest probability of preload responsiveness/unresponsiveness. **Study Design and Methods:** We retrospectively analyzed a prospectively collected convenience sample of hypoperfused adult emergency department (ED) patients. Doppler measurements were obtained before and during a preload challenge using a wireless, wearable Doppler ultrasound system. Based on internal jugular and carotid artery Doppler surrogates of CVP and SV, respectively, we placed hemodynamic assessments into quadrants (Q_x) prior to preload augmentation: low CVP with normal SV (Q_1), high CVP and normal SV (Q_2), low CVP and low SV (Q_3) and high CVP and low SV (Q_4). The proportion of preload responsive and unresponsive assessments in each quadrant was calculated based on the maximal change in ccFT (Δ) during either a passive leg raise or rapid fluid challenge. **Results:** We analyzed 41 patients (68 hemodynamic assessments) between February and April 2021. The prevalence of each phenotype was: 15 (22%) in Q_1 , 8 (12%) in Q_2 , 39 (57%) in Q_3 , and 6 (9%) in Q_4 . Preload unresponsiveness rates were: Q_1 , 20%; Q_2 , 50%; Q_3 , 33%, and Q_4 , 67%. **Interpretation:** Even fluid naïve ED patients with sonographic estimates of low CVP have high rates of fluid unresponsiveness, making dynamic testing valuable to prevent ineffective IVF administration.

Keywords

fluid responsiveness, fluid tolerance, carotid Doppler, venous Doppler, functional hemodynamic monitoring, passive leg raise

Background

In the emergency department (ED), intravenous (IV) fluids are increasingly guided by venous or arterial measurements from point-of-care ultrasound.¹ Although the respiratory variation of the inferior vena cava (IVC)² is a surrogate of central venous pressure (CVP)³ and is an accepted method for estimating right ventricular systolic pressure during echocardiography,⁴ there is an inconsistent relationship between absolute CVP and an increase in cardiac output or stroke volume (SV) after IV fluid administration. For instance, 25% of patients with a CVP ≤ 5 mm Hg,⁵ 40% of patients with a CVP ≤ 8 mm Hg⁶ and 20% of patients with an IVC collapse of $\geq 25\%$ ⁷ are reported to be preload unresponsive. This means that a clinically significant fraction of patients with low venous pressure do not have the intended response to IV fluid.⁸

One arterial ultrasound measure used to guide IV fluid is the corrected flow time of the carotid artery (ccFT).^{9,10} This relies

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on the direct relationship between the duration of systole and SV—an association made in the mid-20th century by Weissler et al.¹¹ Despite the ccFT having excellent diagnostic accuracy for predicting preload responsiveness reported in a recent meta-analysis,¹⁰ much of this data is based on an absolute ccFT threshold. In other words, a low ccFT (ie, suggesting low SV) predicts preload responsiveness and vice versa. Barjaktarevic and colleagues assessed ccFT from a dynamic approach, finding that a +7 millisecond (ms) ccFT change (ccFT_Δ) induced by passive leg raise (PLR) best-dichotomized preload responders from nonresponders.¹²

Often venous and arterial ultrasound measures described above are performed in isolation, however, it has been argued that they should be assessed in tandem by a wireless, wearable Doppler device.^{13–16} Simultaneous Doppler ultrasound of the jugular vein (ie, CVP surrogate) and carotid artery (ie, SV surrogate) create a “Doppler Starling curve”^{15,16} which roughly resembles the canonical “Frank-Starling” curve, but can be non-invasively derived at the bedside. By dichotomizing jugular venous Doppler morphology into “low” and “high” CVP surrogates and ccFT into “low” and “normal” SV surrogates, the Doppler Starling curve is divided into 4 quadrants that phenotype hypoperfused patients.¹⁵

Our objectives were to determine the prevalence of each hemodynamic profile and to determine the rate of preload unresponsiveness for each profile. We had four hypotheses with respect to this novel Doppler Starling curve in fluid naïve, hypoperfused ED patients. First, we predicted that most assessments would fall into the quadrants defined by a “low CVP” jugular Doppler morphology given that these were ED patients studied early in their care. Second, we anticipated that all assessments defined by low CVP would have a 20% to 40% preload unresponsiveness rate given what is known from the CVP and IVC collapse literature. Third, we expected that the assessments beginning with low CVP and normal SV Doppler surrogates would have the highest proportion of preload responsiveness. Finally, we predicted that the quadrants defined by high CVP jugular morphology would have preload unresponsive rates comparable to the intensive care unit (ICU) population (ie, at least 50% unresponsive).¹⁷

Methods

Ethics Approval and Consent

Written and informed consent was obtained from all patients or their next of kin; the study was approved by the Peoria Institutional Review Board (# 1697834-5) and performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments.

Study Design

We performed a post hoc analysis of a prospective, observational study assessing the use of a Doppler ultrasound device to determine preload responsiveness in patients in the ED. We recruited a

convenience sample of patients between February and April 2021 from a community ED who were deemed to need IV fluid resuscitation by the treating clinician. The provider was blinded to the results of the wearable ultrasound. No sample size calculation was performed for this feasibility study.

Eligibility Criteria

Adult patients were enrolled if the treating clinician determined that IV fluid expansion was indicated to correct hypoperfusion. Exclusion criteria were: less than 18 years old, absent informed consent, unable to cooperate with a Doppler ultrasound assessment of the carotid artery (eg, delirium, confusion, excessive phonation, etc) or if there were anatomical contraindications precluding assessment of at least one carotid artery (eg, known bilateral carotid stenoses of at least 70%, bilateral internal jugular central lines, c-spine collar, etc). There was no exclusion for patients with atrial fibrillation, low ejection fraction, or diastolic dysfunction.

Wearable Doppler Ultrasound

The ultrasound patch (Flosonics Medical, Sudbury, ON, Canada) is a wearable, wireless, FDA-cleared, continuous-wave 4 MHz ultrasound. Adhesive straps fix the transducer angle relative to the direction of carotid blood flow.¹⁸ The wearable ultrasound displays real-time carotid corrected flow time (ccFT) (Figure 1) and, when placed over an area of anatomical overlap between the carotid and internal jugular vein, displays the internal jugular vein Doppler spectrogram.¹⁹ Placement of the device entails applying the 2 cm transducer face perpendicular to the trachea at the level of the cricoid cartilage. The device is moved laterally until the point of greatest carotid audio and visual signal is obtained via the iOS device to which the transducer is wirelessly paired. The device is then fixed in place via its incorporated adhesive.

Preload Augmentation

Baseline venous and arterial Doppler spectrograms were obtained in the semi-Fowler position at 45°. Prior to preload augmentation, at least 30 s of continuous Doppler spectrograms were acquired. As previously described,²⁰ preload augmentation was at the discretion of the treating clinician and could be either a 2-min PLR or rapid fluid challenge of at least 250 mL (~4 mL/kg) administered at 100 mL/minute. Doppler spectrograms were recorded continuously throughout the entire preload challenge.

Venous Doppler Analysis

The baseline (ie, semi-Fowler) venous Doppler spectrograms were analyzed qualitatively based on the framework put forth by Kenny et al¹⁹ and Tang²¹ which is illustrated in Figure 2. Briefly, from low-to-high preload the jugular venous Doppler spectrogram progresses from a “continuous” or “pulsatile-fused” morphology

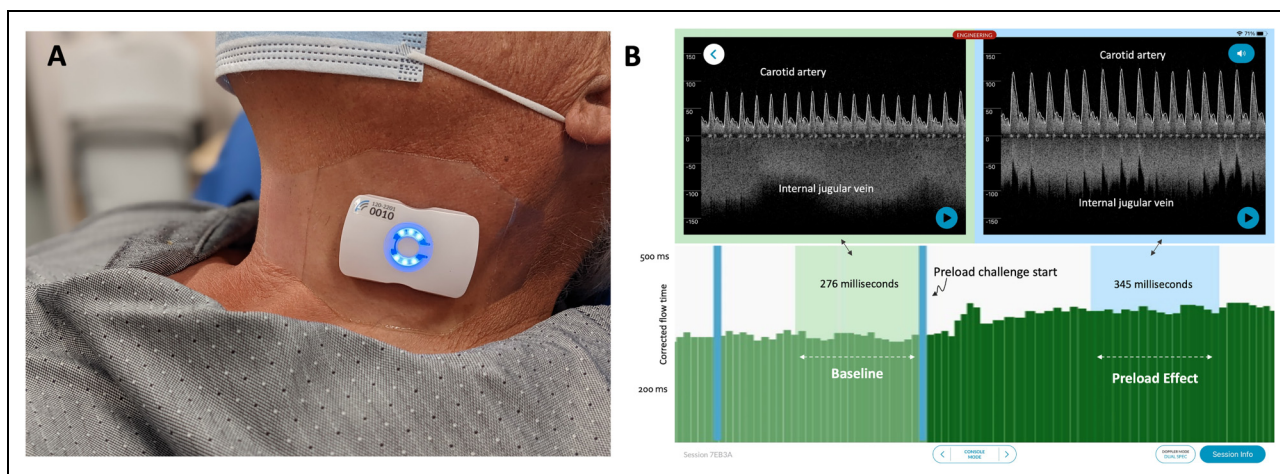


Figure 1. The wireless, wearable Doppler biosensor and user interface. (A) The device on a subject. (B) The user interface of the wearable Doppler showing the carotid artery and jugular Doppler simultaneously; below the spectrograms are the corrected flow time of the carotid artery (ccFT) per cardiac cycle during a preload challenge. This example shows a continuous jugular Doppler morphology with low baseline ccFT (ie, 276 milliseconds) or quadrant 3 (Q3). This example was preload responsive as the ccFT increased by 69 milliseconds. The ccFT is the duration of mechanical systole in milliseconds, corrected for heart rate by the equation of Wodey³⁸.

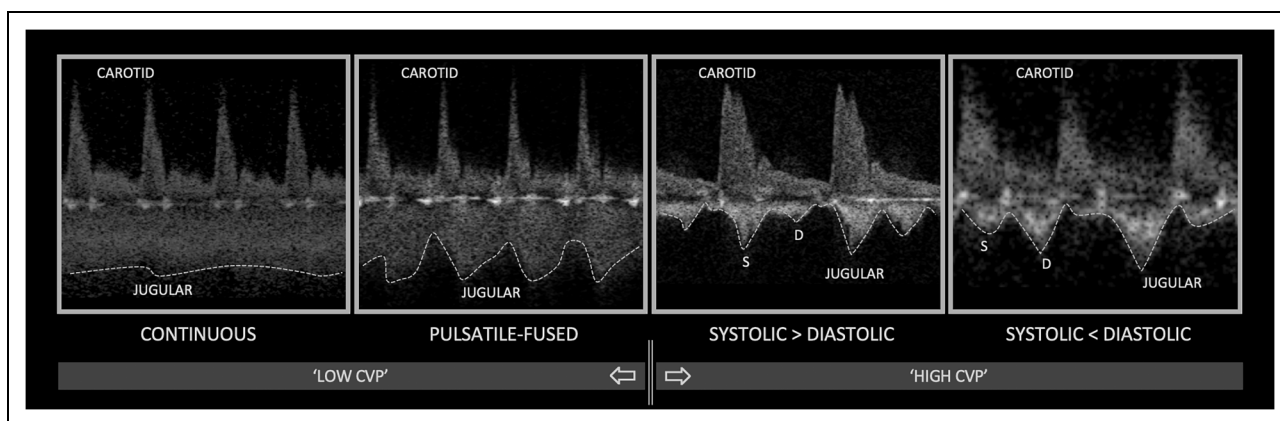


Figure 2. Venous Doppler analysis: this figure shows the scoring system for the internal jugular vein Doppler. “Pulsatile-fused” refers to fusion of the systolic (S) and diastolic (D) waves, that is, the v-wave is not great enough to cleave the S and D waves as seen at higher CVP. This scoring system is dependent on patient position, for instance, $S > D$ is common in healthy volunteers when supine or head down¹⁹, however, not in the upright position.

toward a velocity profile that recapitulates the central venous pressure trace—with the x - and y -descents forming venous Doppler systolic “S” and diastolic “D” waves, respectively. These venous spectrogram changes have been described in the jugular vein,^{22–24} superior vena cava,²⁵ IVC,²⁶ hepatic veins,²⁷ and the femoral vein.²⁸ The relationship between jugular Doppler and the central venous pressure trace has been previously reviewed.²⁴ Three experts in venous Doppler interpretation (R.P., P.R., and K.H.) identified the jugular venous morphology at baseline for each preload challenge by consensus; each expert was blind to the results of the preload challenge and each other. A Fleiss Kappa score was calculated to assess agreement between the blinded experts.

It was previously shown¹⁹ that all healthy volunteers display a “continuous” or “pulsatile fused” jugular venous Doppler

morphology with low preload, whereas systolic (S) > diastolic (D) wave jugular Doppler was only ever observed with increased preload. Given these findings, we categorized the “continuous” and “pulsatile fused” jugular venous Doppler morphology as “low” CVP; “high” CVP is considered $S > D$ morphology or greater (ie, $S > D$; $S = D$; $S < D$ or monophasic D) when patients are in the semirecumbent position (Figure 2). Venous Doppler spectrograms were interpreted at the point of minimum jugular velocity, which corresponds to end-expiration (ie, when the jugular vein rounds out) in spontaneously breathing patients.²⁹

Arterial Doppler Analysis

The carotid arterial Doppler spectrograms were analyzed for the ccFT at baseline (ie, to place the assessment on the Doppler

Starling curve) and $ccFT_{\Delta}$ (ie, to determine preload responsiveness/unresponsiveness) from baseline to peak effect during preload challenge. The number of cardiac cycles averaged before and during preload augmentation was dictated by the coefficient of variation of each particular measure to ensure change could be detected with statistical confidence.³⁰ The device software is able to perform these arterial calculations in real-time, however, all data was analyzed later, offline, given that venous Doppler interpretation was required per above. The primary determinant of whether or not a patient was deemed preload responsive was the threshold reported by Barjaktarevic et al (ie, +7 ms $ccFT_{\Delta}$).¹²

Doppler Starling Curve

To place patients on the Doppler Starling curve in the baseline position, each assessment was parsed into “low” or “high” CVP morphology per above; this dichotomy defined the *x*-axis of the Doppler Starling curve. For the *y*-axis, Kenny et al. have previously shown that prior to PLR in healthy volunteers, the average $ccFT$ based upon Wodey’s equation was 310 ± 10 ms in the semirecumbent position.³¹ We therefore used this value as a surrogate to dichotomize “low” from “normal” SV on the *y*-axis from arterial Doppler taken simultaneously with the venous Doppler. Accordingly, the “Doppler Starling curve” is composed of 4 quadrants (Figure 3). Quadrant 1 (Q_1) is defined by patients with a “low” CVP jugular morphology and a baseline $ccFT \geq 310$ ms. Quadrant 2 (Q_2) comprises patients with a “high” CVP jugular morphology and baseline

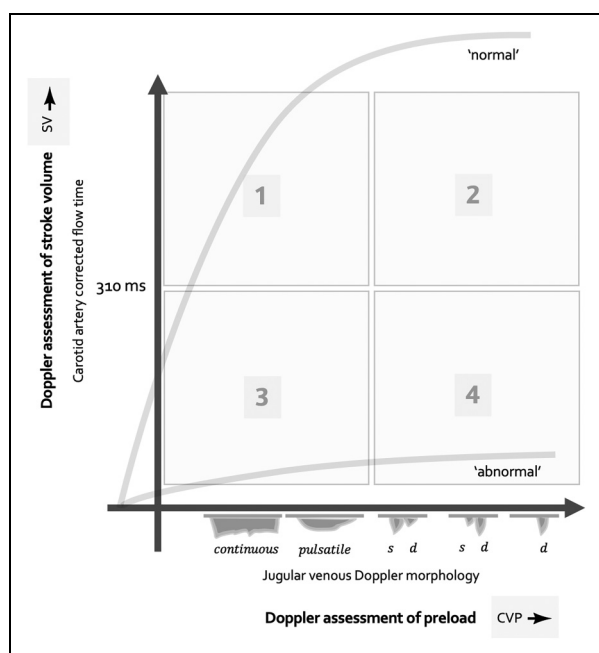


Figure 3. The Doppler Starling curve. See the text for how quadrants 1 to 4 are defined. The two curves depicted represent extremes, there are an infinite number of possible curves between them.

$ccFT \geq 310$ ms. Quadrant 3 (Q_3) are patients with “low” CVP jugular Doppler and a baseline $ccFT < 310$ ms while quadrant 4 (Q_4) are patients with “high” CVP jugular Doppler and a baseline $ccFT < 310$ ms (Figure 3). Placing patients in the baseline Doppler Starling quadrant was performed offline given that human interpretation of the jugular venous morphology is required. We performed chi-squared testing to assess interactions between preload responsiveness and quadrant number and preload responsiveness versus “low” or “high” CVP jugular venous pattern.

Results

Patients

In total 53 patients were enrolled. Twelve patients (23%) were entirely excluded for poor arterial or venous Doppler signal (ie, no clear diastolic notch or absent venous Doppler signals); 41 patients and 68 assessments comprise this analysis. The disposition of the patients in this analysis from the ED included: 12% to the ICU; 61% to the general medical or surgical floor; 5% to the short-stay unit, and 22% discharged from the ED. The 28-day readmission and mortality rates for the 41 patients were 24% and 5%, respectively. The baseline clinical characteristics of the 41 included patients are listed in Table 1. The breakdown in these clinical characteristics for each of the 4 quadrants is shown in supplemental e-Table 1.

Doppler Starling Curve

In the baseline, semirecumbent (ie, semi-Fowler) position, 15 (22%) assessments were in Q_1 (ie, low CVP, normal SV surrogates). Q_2 (ie, high CVP, normal SV surrogates) included 8 (12%) assessments. Q_3 (ie, low CVP, low SV surrogates) included 39 (57%) assessments. Finally, Q_4 (ie, high CVP, low SV surrogates) included 6 (9%) assessments.

Fifty-four (79%) assessments were in either Q_1 or Q_3 (ie, low CVP surrogate) while the remaining 14 (21%) assessments were in either Q_2 or Q_4 (ie, high CVP surrogate). Twenty-three (34%) assessments were initially categorized being in Q_1 or Q_2 (ie, normal $ccFT$, SV surrogate) while the remaining 45 (66%) were in either Q_3 or Q_4 (ie, low $ccFT$, SV surrogate). The Fleiss Kappa coefficient for agreement between experts was moderate at 0.44 (ie, moderate agreement).

Preload Responsiveness Versus Unresponsiveness

The fraction of assessments with preload responsiveness and unresponsiveness based on the +7 ms $ccFT_{\Delta}$ threshold for each quadrant is shown in Figure 4. Tables 2 and 3 break down these fractions based upon other baseline measures. By chi-squared testing, there was no statistically significant difference between preload responsiveness and quadrant number ($p = .18$) nor between preload responsiveness and “low” (ie, Q_1 and Q_3) versus “high” (ie, Q_2 and Q_4) CVP jugular venous patterns ($p = .07$).

Table 1. Baseline Patient Characteristics.

Number of patients	41
Female sex, <i>n</i> (%)	24 (59%)
Age, mean (SD)	62 (17.5)
Body mass index (SD)	29.3 (7.8)
IV fluids prior to enrollment (mL/kg), mean (SD)	1.6 (3)
Comorbidities, <i>n</i> (%)	
Congestive heart failure	5 (12%)
Ejection fraction*, mean (SD)	57.2 (14.7)
Chronic kidney disease	7 (17%)
Chronic obstructive pulmonary disease	9 (22%)
Diabetes	11 (27%)
Cirrhosis	1 (2%)
Malignancy	3 (7%)
Immunosuppressed**	9 (22%)
Presentation	
Infection or sepsis suspected, <i>n</i> (%)	33 (80%)
Heart rate (beats per minute), mean (SD)	102 (22.4)
Mean arterial pressure (mm Hg), mean (SD)	79 (18.2)
Temperature (°C), mean (SD)	37.4 (1.0)
Oxygen saturation (%), mean (SD)	96 (3)
Corrected flow time (ms), mean (SD)	296 (27)
Indication for IV fluids, <i>n</i> (%)	
Hypotension	31 (76%)
Tachycardia	27 (66%)
Low urine output	0 (0%)
Acute kidney injury	10 (24%)
Elevated lactate	8 (20%)
Confusion	4 (10%)
Other	29 (71%)

*Ejection fraction within 12 months of ED presentation, if available.

**Defined as active malignancy, AIDS or receiving immunosuppressive medications.

Discussion

Precision fluid management is challenging during resuscitation; noninvasive approaches that link fundamental physiology to the bedside could enhance clinical practice. Thus, our observational, pilot study is important from three perspectives: (1) our data supports the conceptual framework of a “Doppler Starling curve,” (2) we demonstrated it is feasible to noninvasively phenotype hypoperfused ED patients based upon CVP and SV surrogates, and (3) we found that venous-arterial Doppler identified 79% of assessments in our study cohort as having “low CVP” (ie, Q_1 and Q_3) and that 30% of these assessments were preload unresponsive.

From a basic physiology perspective, our hypotheses derive from two fundamental aspects of the Frank-Starling relationship: (1) with increasing preload, there is increasing SV until a plateau is reached³² and (2) there can be a variety of different slopes defining this curve (eg, “steep,” “shallow,” “flat”) as illustrated in Figures 3 and 4. Given the general shape of the Starling relationship (ie, initial upslope followed by flattening), preload responsiveness should be more likely when CVP is low (eg, Q_1 and Q_3), however, it is not guaranteed; a plateau can be reached with low preload and this phenotype is expected to be more common in Q_3 .¹⁵ For example, if we restrict our analysis to patients with low CVP jugular Doppler morphology at

baseline (ie, Q_1 and Q_3), the unresponsiveness rate is 30% which is consistent with CVP and IVC collapse literature.^{5,7} If we refine these patients further, unresponsiveness was more common in Q_3 than in Q_1 , which is predicted by the shape of the Starling curve, though this difference was not statistically significant. On the other hand, “high CVP” jugular morphology at baseline predicted a fluid unresponsiveness rate comparable to the ICU (ie, at least 50%).⁵ While these differences were not statistically significant, our pilot investigation was underpowered and conceptualized as hypothesis-generating.

At the bedside, the 4 quadrants of the Doppler Starling curve may help the clinician narrow the pretest probability for preload responsiveness prior to performing a preload challenge (eg, PLR or rapid fluid challenge) and track the Doppler Starling curve in real-time. For example, a hypotensive patient with a baseline ccFT of 275 ms and a continuous jugular morphology is placed in Q_3 . Though there is a “low CVP” jugular Doppler, this patient still has a 33% chance of being preload unresponsive, consistent with CVP data.⁵ When a PLR is performed (Supplemental Video 1), the ccFT falls consistent with preload unresponsiveness. Furthermore, during the PLR, the jugular venous morphology transitions to a “high CVP” pattern; the patient moves from Q_3 to Q_4 during the preload challenge and this simplifies the cumbersome workload typically required when performing a PLR with Doppler ultrasound.³³ Additionally, the baseline Doppler Starling quadrant could hint at the etiology of hypoperfusion. For example, a hypotensive patient in Q_1 suggests vasodilation while in Q_4 , cardiac dysfunction is highly likely. Additional research should be directed at this question and especially this constellation of low ccFT with high CVP pattern.

Limitations

The key limitation of this pilot investigation is that we did not measure CVP or SV. In theory, the same framework could be used in conjunction with direct measures of CVP and SV or other ultrasonographic surrogates (eg, IVC size/variation, left ventricular outflow tract velocity time integral). Absolute ccFT as a proxy for SV is a limitation requiring specific elaborations. First, although there is a direct relation between systolic time and SV,^{11,34} systolic time is also affected by afterload and contractility.^{35,36,37} Accordingly, the absolute value of ccFT is analogous to pulse pressure. A low absolute ccFT (or pulse pressure) suggests diminished SV and vice versa, but these relationships are mediated by other competing variables; therefore, a dynamic measure (eg, ccFT_Δ during a preload challenge¹²) adds important hemodynamic data regarding the slope of the cardiac function curve. Additionally, when comparing absolute ccFT between investigations, the value obtained by the equations of Bazett versus Wodey is not interchangeable^{38,39}; the latter was used in this analysis. Only moderate agreement between the blinded observers for dichotomizing the jugular venous morphology into “low” versus “high” CVP patterns is another important limitation. Nearly all of the disagreement was distinguishing between the “pulsatile fused” and “S>D wave” jugular morphologies, that is the jugular venous

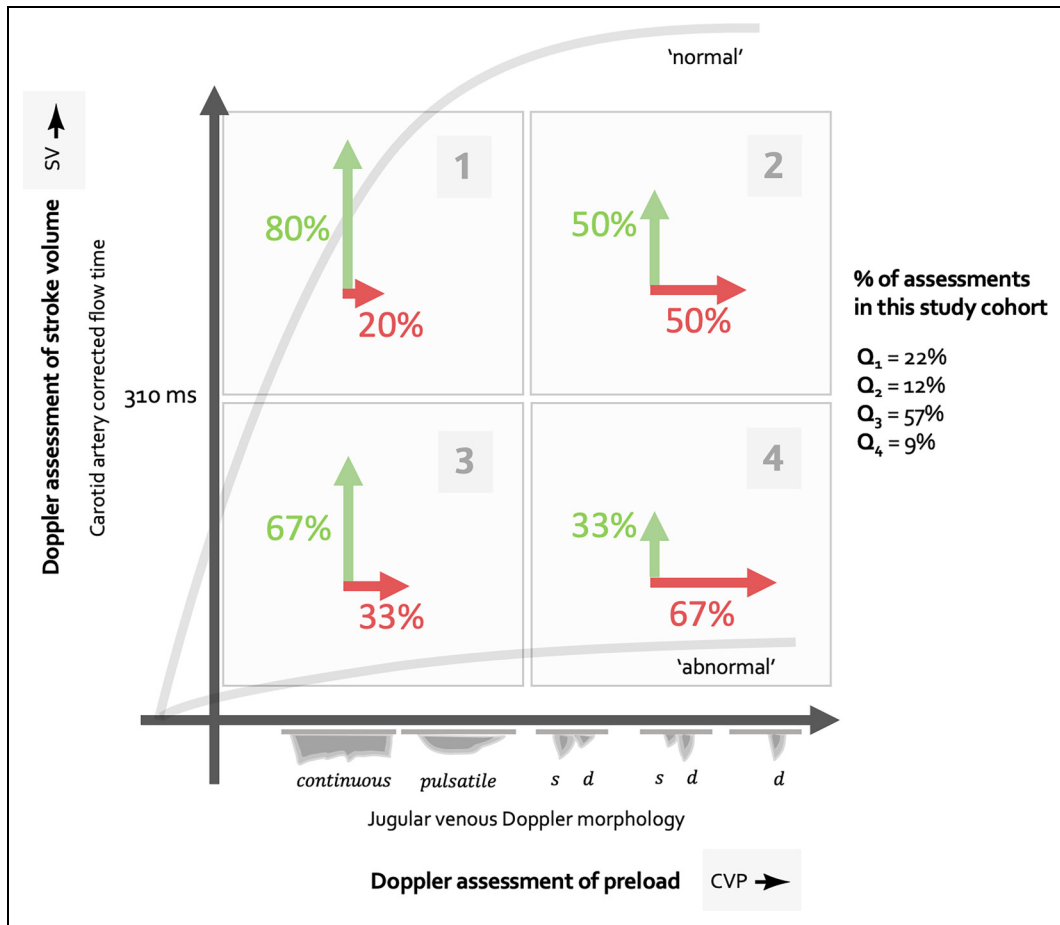


Figure 4. The fraction of preload responsive and unresponsive assessments per quadrant. The green (vertical) arrow represents the fraction of responsive assessments while the red (horizontal) arrow represents the fraction of unresponsive assessments in each quadrant.

Table 2. Preload Responsiveness per Quadrant. Preload Responsiveness Was Defined by $ccFT_{\Delta}$ During a Preload Challenge.

	Quadrant 1 ($\downarrow$ CVP, $\leftrightarrow$ SV)	Quadrant 2 ($\uparrow$ CVP, $\leftrightarrow$ SV)	Quadrant 3 ($\downarrow$ CVP, $\downarrow$ SV)	Quadrant 4 ($\uparrow$ CVP, $\downarrow$ SV)
Responsive	80%	50%	67%	33%
Unresponsive	20%	50%	33%	67%

Abbreviations: CVP, central venous pressure; SV, stroke volume.

Table 3. The Fraction of Responsive and Unresponsive Patients Based upon CVP or SV Surrogates Alone. Preload Responsiveness Was Defined by $ccFT_{\Delta}$ During a Preload Challenge.

	Q_1 and Q_3 ($\downarrow$ CVP)	Q_2 and Q_4 ($\uparrow$ CVP)	Q_1 and Q_2 ($\leftrightarrow$ SV)	Q_3 and Q_4 ($\downarrow$ SV)
Responsive	70%	43%	70%	62%
Unresponsive	30%	57%	30%	38%

Abbreviations: CVP, central venous pressure; SV, stroke volume.

signals that border the “low” versus “high” preload conditions. Future studies should include more objective criteria for distinguishing what qualifies S/D wave cleavage. Physiologically, the

distinction between the “pulsatile fused” and “S>D wave” jugular morphologies is a function of the height of the right atrial pressure v-wave. Simultaneous comparison with invasive measures could codify this distinction. This would be particularly interesting in patients with elevated pulmonary pressures in acute and chronic settings (eg, chronic obstructive pulmonary disease and acute pulmonary embolism), though previous investigations have identified right heart dysfunction via Doppler of the internal jugular vein and superior vena cava.^{24,40,41} There were statistical limitations to our study as well. First, repeated measures on the same patients could mean that the measures are not independent. Though physiology changes rapidly in response to various interventions in the ED and, therefore, might be considered an independent phenomenon,

this is not clear cut. Future studies of this framework should include a larger sample size of patients in each of the 4 quadrants without repeated measures. Second, the sample size of our pilot investigation precludes multivariable regression to determine which demographics are associated with the presence of each hemodynamic profile. We suspect that the lack of a statistically significant difference between responsive and unresponsive subjects between the quadrants likely reflects an underpowered investigation. Another potential limitation is that B-mode imaging was not used for placement of the wearable transducer; therefore, positioning was “blind” in this sense. Nevertheless, the CW ultrasound produces a sonic curtain over 2 cm in length, making uniform insonation of all red blood cell velocities across a 6 mm to 7 mm carotid artery very likely when there is good visual and audio feedback from the device.⁴² To the extent that the internal jugular and common carotid arteries are anatomically separated, establishing simultaneous signals from both is problematic and could account for the 12 excluded subjects in whom both signals were unattainable. Because we did not track the number of patients who were excluded (ie, the total source population), bias is introduced if inherent differences between the source population and our study cohort exist. Finally, the reliance on the clinician decision to administer fluid bolus as an inclusion criterion may have introduced selection bias as we are not obtaining a comprehensive set of patients with one clinical entity, but rather, a heterogeneous group of patients.

Conclusions

This pilot data supports the construct of a Doppler Starling curve, the simultaneous assessment of venous and arterial Doppler ultrasound measures during a hemodynamic intervention, and how Doppler ultrasound can help clinicians determine the pretest probability of preload responsiveness during resuscitation. The Doppler Starling framework may also suggest hypo perfusion etiology, and further investigation and validation of this framework are ongoing.

Abbreviations

IV	intravenous
SV	stroke volume
SV _Δ	change in stroke volume
CVP	central venous pressure
PLR	passive leg raise
ED	emergency department
FDA	Food and Drug Administration
ccFT	corrected carotid flow time
ccFT _Δ	change in corrected carotid flow time
VTI	velocity time integral
FT	flow time
RFC	rapid fluid challenge
mL/min	milliliters per minute
mL	milliliters
ms	milliseconds
LVEF	left ventricular ejection fraction
RV	right ventricular
LV	left ventricular

IVC	inferior vena cava
VExUS	venous excess ultrasound score
TTE	transthoracic echocardiography.

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Not applicable.

Authors' Contributions

JESK: conception, study design, analysis and interpretation, and drafting; RP: conception, analysis and interpretation, and critical revisions; PR: conception, analysis and interpretation, and critical revisions; KH: conception, analysis and interpretation, and critical revisions; SOG: data acquisition, analysis and interpretation, and critical revisions; JKE: conception, design, data acquisition, analysis, and critical revisions; CH: analysis and interpretation, and critical revisions; DHJ: data acquisition, analysis, and critical revisions; VCL: conception, data acquisition, analysis and interpretation, and critical revisions; BOK: conception, data acquisition, analysis and interpretation, and critical revisions. All authors read and approved the final manuscript.

Declaration of Conflicting Interests

JESK, SOG, JKE, CH, and DHJ work for Flosionics Medical, the start-up building the wearable Doppler ultrasound. RP, PR, KH, VCL, and BOK declare no competing interests.

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Supplemental Material

Supplemental material for this article is available online.

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